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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
08/916,140	08/21/1997	MATTHEW P. SCOTT	CIBT-P04-203	2613

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BOSTON, MA 02110-2624

EXAMINER
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SCHNIZER, RICHARD A

ART UNIT	PAPER NUMBER
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1635

DATE MAILED: 06/30/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

317

<b>Office Action Summary</b>	<b>Application No.</b> 08/916,140	<b>Applicant(s)</b> SCOTT ET AL.	
	<b>Examiner</b> Richard Schnizer, Ph. D	<b>Art Unit</b> 1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --  
**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
  - If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
  - If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
  - Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on 12 April 2004.
- 2a) ☐ This action is **FINAL**.                      2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 61,62,70,71 and 81 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☒ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 61,62,70,71 and 81 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☒ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 29 January 2002 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.  
 Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
 Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All    b) ☐ Some \*    c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

- |   |   |
|---|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)   | 4) <input type="checkbox"/> Interview Summary (PTO-413)<br>Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)  | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152)             |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)<br>Paper No(s)/Mail Date <u>12/17/98</u> . | 6) <input type="checkbox"/> Other: _____  |

## **DETAILED ACTION**

### ***Continued Examination Under 37 CFR 1.114***

An amendment was received and entered on 4/12/04.

Claims 63-69 and 72-80 were canceled as requested.

Claims 61, 62, 70, 71, and 81 remain pending and under consideration in this Office Action.

Previously, it was indicated that claim 61 was allowable. After further search and consideration, this indication is withdrawn.

### ***Drawings***

Applicant has submitted drawings which are adequate for the purpose of examination.

### ***Information Disclosure Statement***

Applicant filed an information disclosure statement on 12/17/98. Although all of the documents filed therein were considered, the Examiner inadvertently failed to initial the Gorlin reference ('DO') on the last page. A new copy of the IDS with all references initialed is attached.

### ***Compliance with Sequence Rules***

In the amendment filed 4/12/04, Applicant amended the specification include SEQ ID NOS: for sequences at pages 32 and 39. However, the Office has not received

a new Sequence Listing in either paper or CRF form. Further at page 40 of the specification, Table 1 continues to contain a large number of sequences that are not identified by SEQ ID NO but which are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 CFR 1.821(a)(1) and (a)(2). See the column labeled 'Primers'. As a result the application clearly fails to comply with the requirements of 37 C.F.R. 1.821-1.825. Applicant's attention is directed to the final rule making notice published at 55 FR 18230 (May 1, 1990), and 1114 OG 29 (May 15, 1990). If these sequences are listed in the current Sequence Listing, then the specification should be amended to include the appropriate SEQ ID NOS in the Table. If these sequences are not in the current Sequence Listing, then Applicant must provide:

A substitute computer readable form (CRF) copy of the "Sequence Listing".

A substitute paper copy of the "Sequence Listing", as well as an amendment directing its entry into the specification.

A statement that the content of the paper and computer readable copies are the same and, where applicable, include no new matter, as required by 37 C.F.R. 1.821(e) or 1.821(f) or 1.821(g) or 1.825(b) or 1.825(d).

For questions regarding compliance to these requirements, please contact:

For Rules Interpretation, call (703) 308-4216

For CRF Submission Help, call (703) 308-4212

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***Priority***

Claims 61, 71, 72, and 81 include method steps requiring the use of cells that express wild type patched to identify agents that decrease hedgehog signaling. Such assays find support in US Patent 5,837,538, filed 10/6/1995, at column 7, lines 56 to column 8, line 40. These assays are not supported in the parent document, 09/319,745, filed 10/7/1994. As such, the effective filing date for claims 61, 71, 72, and 81 is 10/6/1995.

***Claim Rejections - 35 USC § 112***

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 61, 62, 71, and 81 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for methods of measuring hedgehog signal transduction or *patched* activity in cells that have been contacted with a *hedgehog* protein does not reasonably provide enablement for measuring *hedgehog* signal transduction or *patched* activity in cells that have not been contacted with a *hedgehog* protein. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

Claims 61 and 81, and an embodiment of claim 71, require the measurement of *hedgehog* signal transduction in cells. Claim 70, not included in this rejection, is drawn to embodiments of claim 61 in which the cells comprising functional patched are contacted by a *hedgehog* protein. If claim 70 further limits claim 61, then claim 61 embraces embodiments in which *hedgehog* signal transduction is measured without contacting the cells with *hedgehog*. The specification and the prior art teach that *hedgehog* functions by binding to *patched*. This results in initiation of the *hedgehog* signal transduction cascade which has several measurable endpoints including expression of many genes and the stimulation of cellular proliferation. It follows that in cells comprising functional *patched*, *hedgehog* signal transduction cannot take place unless *hedgehog* binds *patched*, the specification has not taught any such conditions, and none are apparent in the prior art of record. In the absence of guidance or working examples in the specification or the prior art, one of skill in the art would have to perform undue experimentation in order to invent or discover means to cause *hedgehog* signal transduction in the absence of *hedgehog* protein. As such, one could not practice the invention commensurate in scope with the claims without undue experimentation.

Claim 62, and an embodiment of claim 71, require measurement of “patched activity” in cells. As discussed above, the “activity” of *patched* is to bind *hedgehog* and initiate signal transduction. The specification also discusses the activity of *patched* as a transmembrane transporter or channel, however, it fails to disclose what *patched* transports, and the pre-and post-filing art do not teach that *patched* functions as either a

transporter or a channel. As such, the only enabled measurements of *patched* activity disclosed in the specification are limited to those involved in *hedgehog* signal transduction, i.e. binding and release of *hedgehog*. Neither the specification nor the prior art of record provide any guidance as to how to measure of these activities without contacting the cell with *hedgehog*. In the absence of guidance or working examples in the specification or the prior art, one of skill in the art would have to perform undue experimentation in order to invent or discover means to measure *patched* activity in the absence of *hedgehog* protein. As such, one could not practice the invention commensurate in scope with the claims without undue experimentation.

### ***Claim Rejections - 35 USC § 102***

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

Claims 61 and 70 are rejected under 35 U.S.C. 102(a) as being anticipated by Fan et al (Cell 81(3): 457-465, 5/5/1995).

Fan taught that addition of forskolin, IBMX or db-cAMP to cultured mouse embryonic mesoderm explants completely blocked sonic hedgehog-mediated induction of Pax1 and Mtwist expression. See paragraph bridging pages 460 and 461; first full paragraph on page 461; and Fig 4 on page 461. Addition of these reagents also

blocked sonic hedgehog-mediated increases in DNA synthesis. See second full paragraph on page 461.

Thus Fan anticipates the claims.

### ***Conclusion***

No claim is allowed.


Any inquiry concerning this communication or earlier communications from the examiner(s) should be directed to Richard Schnizer, whose telephone number is 571-272-0762. The examiner can normally be reached Monday through Friday between the hours of 6:20 AM and 3:50 PM. The examiner is off on alternate Fridays, but is sometimes in the office anyway.

If attempts to reach the examiner by telephone are unsuccessful, the Examiner's supervisor, John Leguyader, be reached at 571-272-0760. The official central fax number is 703-872-9306. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent application status and history information. It also enables applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public.

For all other customer support, please call the USPTO Call Center (UCC) at 800-786-9199.

Richard Schnizer, Ph.D.



DAVE T. NGUYEN  
PRIMARY EXAMINER